

human subject in a manner that reduces signaling of the VEGFR-3 polypeptide encoded by the allele; and correlating presence or absence of said mutation in the nucleic acid to a risk of developing hereditary lymphedema, wherein presence of said mutation in the nucleic acid correlates with an increased risk of developing hereditary lymphedema, and wherein absence of said mutation in the nucleic acid correlates with no increased risk of developing hereditary lymphedema.

2. [Amended] A method according to claim 1 or claim 37 wherein the assaying step comprises assaying for a mutation altering a tyrosine kinase domain amino acid sequence of the protein encoded by the VEGFR-3 allele.

3. [Amended] A method according to claim 1 or claim 37 wherein the assaying step comprises assaying for a missense mutation in a VEGFR-3 allele at a position corresponding to one of codons 857, 1041, 1044 and 1049 of the VEGFR-3-encoding sequence set forth in SEQ ID NO:1.

4. [Amended] A method according to claim 1 or claim 37 wherein the assaying step comprises assaying for a missense mutation in a VEGFR-3 allele at a position corresponding to codon 1114 of the VEGFR-3-encoding sequence set forth in SEQ ID NO:1.

5. [Amended] A method according to claim 1 or claim 37 wherein said method comprises at least one procedure selected from the group consisting of:

- (a) determining a nucleotide sequence of at least one codon of at least one VEGFR-3 allele of the human subject;
- (b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;
- (c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and
- (d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

6. [Amended] A method according to claim 1 or claim 37 wherein said method comprises: performing a polymerase chain reaction (PCR) to amplify nucleic acid comprising VEGFR-3 coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

7. [Amended] A method of screening for a VEGFR-3 hereditary lymphedema genotype in a human subject, comprising the steps of:

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(a) providing a biological sample comprising nucleic acid from said subject, said nucleic acid including sequences corresponding to said subject's VEGFR-3 alleles;

(b) determining a VEGFR-3 genotype by analyzing said nucleic acid for the presence of a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele, wherein the presence of a mutation altering the encoded amino acid sequence of at least one VEGFR-3 allele of the human subject in a manner that reduces signaling of the VEGFR-3 polypeptide encoded by the allele identifies a hereditary lymphedema genotype.

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14. [Amended] An oligonucleotide useful as a probe for identifying polymorphisms in a human Flt4 receptor tyrosine kinase gene, the oligonucleotide comprising 6-50 nucleotides that have a sequence that is identical or exactly complementary to a portion of a human VEGFR-3 coding sequence set forth in SEQ ID NO:1, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution.

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20. [Amended] An array of oligonucleotide probes immobilized on a solid support, wherein each probe occupies a separate known site in the array; and wherein the array includes at least one probe set comprising two to four probes, wherein one probe is exactly identical or exactly complementary to human VEGFR-3 coding sequence set forth in SEQ ID NO:1, and the other one to three members of the set are exactly identical to the first member, but for at least one different nucleotide, which different nucleotide is located in the same position in each of the one to three additional set members.

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